U.S. Department of Energy
Washington, D.C.

ORDER

DRAFT
DOE O 443.1A

Approved: XX-XX-06

SUBJECT: PROTECTION OF HUMAN SUBJECTS

1. OBJECTIVE. To establish Department of Energy (DOE) procedures and responsibilities for implementing the policy and requirements set forth in 10 Code of Federal Regulations (CFR) Part 745, Protection of Human Subjects; and in DOE P 443.1, *Protection of Human Subjects*, dated 05-15-00.

2. CANCELLATION. This Order cancels DOE Order 443.1, *Protection of Human Subjects*, dated 5-15-00. Cancellation of an Order does not by itself modify or otherwise affect any contractual obligation to comply with the Order. Contractor Requirements Documents (CRDs) containing directive requirements that have been applied to a contract remain in effect until the contract is modified to eliminate or replace requirements from canceled directives.

3. APPLICABILITY.

   a. DOE Elements. Except for exclusions in paragraph 3d, this Order applies to all Departmental elements (Attachment 1 or online at www.directives.doe.gov) and automatically applies to DOE elements created after it is issued.

      The National Nuclear Security Administration (NNSA) Administrator will assure that NNSA employees and contractors comply with their respective responsibilities under this directive.

   b. DOE Contractors. Except for the exclusions in paragraph 3d, the CRD (Attachment 2) sets forth requirements to be applied to contracts that involve human subjects research (HSR) as defined in paragraph 6e, and comprehensively explained in DOE P 443.1, irrespective of the party conducting the HSR under the contract.

   c. Other Contracts and Agreements. The requirements of this Order will be applied to HSR conducted with DOE funding, at DOE institutions, or by DOE personnel under agreements other than site/facility management contracts, such as support services contracts, grants, cooperative agreements, work-for-others agreements, and interagency agreements.

   d. Exclusions. None.

4. REQUIREMENTS.

   a. Approvals. No HSR conducted with DOE funding, at DOE institutions, or by DOE personnel may be initiated without both a Federalwide Assurance (FWA)

and approval by the cognizant Institutional Review Board (IRB) in accordance with 10 CFR 745.103.

b. Solicitations. Any solicitation for research involving human subjects must indicate the applicable requirements of this Order, 10 CFR 745, and 45 CFR 46.

c. Agreements. Any DOE contract, financial assistance agreement, or other agreement involving HSR must prescribe compliance with this Order, 10 CFR 745, and 45 CFR 46. See also CRD (Attachment 2).

d. Notification. DOE HSR Program manager must be notified of any new solicitation or proposal involving HSR (including personally identifiable information or materials) that addresses:

(1) an institution without an established IRB;

(2) a foreign country;

(3) a potential for significant controversy (e.g., negative press or reaction from stakeholder or oversight groups);

(4) research subjects in a protected class; or

(5) the generation or use of classified or sensitive unclassified information;

(6) current or former DOE employees or DOE contractor employees.

e. Reporting.

(1) HSR projects must be reported annually to the DOE HSR Projects Database, in accordance with directions and schedules provided by HSR Program manager.

(2) The HSR Program manager will be notified of:

(a) Adverse events, unanticipated risks, and complaints about the research, with a description of corrective actions taken and/or to be taken;

(b) Changes to IRB membership;

(c) Suspension or termination of IRB approval of research;

(d) Known or potential incidents of non-compliance with requirements of this Order, 10 CFR 745, 45 CFR 46, and any approved plan for correcting a non-compliance.

f. Waivers. Requests for waivers from the requirements of 10 CFR 745 or this Order must be submitted to HSR Program manager in writing. A waiver may be granted provided it is not prohibited by law and does not present an undue risk to the health and safety of workers or research volunteers. Waiver decisions must set forth in writing the basis for granting or denying the request.

g. Protected Classes. Research involving pregnant or lactating women, children, prisoners, or the mentally disabled must be conducted in accordance with 45 CFR 46 Subparts B, C, and D.

5. RESPONSIBILITIES.

a. Director of the Office of Science.

(1) Implements 10 CFR 745 within the Department in accordance with policy established by the Secretary and DOE P 443.1.

(2) Determines what constitutes DOE-related HSR.

(3) Ensures implementation of human research subject protection.

(4) Designates the HSR Program manager.

b. DOE HSR Program manager .

(1) Develops and implements procedures for the DOE HSR program.

(2) Prepares and updates guidance to be followed for obtaining approval for HSR.

(3) Reviews/approves local plans to correct any noncompliance with applicable HSR requirements, or to mitigate adverse study events.

(4) Provides advice and guidance on evolving DOE and national bioethics and regulatory issues regarding human research subjects protection and helps identify and resolve program/project concerns.

(5) Develops and conducts educational programs on bioethics and human research subjects protection requirements, practices, and procedures relevant to DOE employees, DOE contractor personnel, financial assistance recipients, and the public.

(6) Regularly conducts institutional performance reviews to assess compliance with human research subjects protection requirements.

(7) Serves as the Chair of the DOE Human Subjects Working Group and as the official DOE representative to groups with bioethics and HSR interests.

(8) Reviews and approves requests for waivers to requirements of 10 CFR 745, and satisfies the advance notice and publication requirements of 10 CFR 745.101(i) prior to granting any waiver.

(9) Concurs in HSR provisions in interagency agreements.

(10) Maintains the HSR Projects Database for the Department.

c. Program Secretarial Officers (PSOs), NNSA Administrators and Heads of Field Organizations (HFOs) or their Designees.

(1) Ensure that all proposals for research, studies, tests, surveys, surveillance, or other data collection are reviewed to identify research involving human subjects.

(2) Ensure that any questions or uncertainties regarding the applicability of human research subjects protection requirements to such proposals, and any other issues and concerns regarding the requirements of this Order, are promptly referred to HSR Program manager for resolution.

(3) Ensure that the contracting officer is advised when work statements for proposed agreements include HSR.

(4) Ensure their staffs and subordinate field elements comply with the requirements of this Order, including the notification requirements in paragraph 4e.

(5) Actively participate in human research subjects protection educational programs.

(6) Assure self-assessments are periodically conducted to verify compliance with the requirements of this Order.

(7) At their discretion, conduct further review and approve or disapprove research that has been approved by the IRB. (Note: PSOs, NNSA Administrators, HFOs, or their designees may not approve HSR that has not been approved by an IRB.) See 10 CFR 745.112..

(8) Ensure appropriate oversight of the administration of research subjects protection programs of contractors and financial assistance recipients under their cognizance, and other parties to DOE agreements, to ensure compliance with applicable human research subjects protection requirements.

(9) Ensure HSR Program manager is involved in negotiating those portions of interagency agreements that address HSR.

(10) Appoint a point of contact for interacting with HSR Program manager on program-related and/or Department-wide issues.

6. DEFINITIONS.

a. Assurance. The written documentation, satisfactory to the Secretary of Energy, required from the prospective performing institution, that ensures institutional compliance with and implementation of DOE and Department of Health and Human Services (DHHS) regulations for the protection of human research subjects. The only documentation currently meeting this requirement is an FWA. See http://www.hhs.gov/ohrp/assurances/assurances_index.html

b. Adverse Effect. A direct result of an administered research protocol (e.g., negative or deleterious drug reaction, collateral damage to the human subject).

c. Adverse Event. A result surrounding or indirectly related to the entire research process (e.g., mishaps, mistakes, incorrect dosage administered, reconsideration of human subject involvement).

d. DOE HSR Projects Database. A compilation of summary information, which is available on the website at**:** http://hsrd.orau.gov/ updated annually, on every HSR project conducted by DOE personnel, with DOE funding, or at DOE institutions or facilities.

e. DOE HSR. Any systematic investigation (including research development, testing, and evaluation) utilizing living individuals or personally identifiable information or materials, designed to develop or contribute to general knowledge. See DOE P 443.1 for examples and exclusions.

f. Institution. Any public or private entity or agency (including Federal, State, and other agencies). For DOE, this term refers to laboratories and other facilities managed by DOE, DOE contractors, or DOE financial assistance recipients.

g. Institutional Review Board (IRB). A committee or board established by an institution that performs initial and continuing reviews of research involving human subjects, and is registered with the Office for Human Research Protections (OHRP) and designated on an FWA.

7. REFERENCES.

a. DOE P 443.1, *Protection of Human Subjects,* dated 05-15-00, which defines DOE policy for the protection of human subjects in research activities.

b. DOE Human Subjects Protection Resource Book, Office of Biological and Environmental Research, 2006.

c. 5 United States Code 552, The Freedom of Information Act (Public Law 89-487 as amended), which establishes the right of citizens to request information from

Federal agencies and establishes a framework of procedures to implement this right.

d. 5 U.S.C. 552a, Privacy Act of 1974 (PL 93-549), as amended, which establishes requirements for the collection, maintenance, and dissemination of personal information by Federal agencies.

e. DOE N 481.1A, *Reimbursable Work for Department of Homeland Security*, dated 4-21-03, contains additional information and direction to cognizant DOE contracting officers and other affected Federal and contractor personnel identifying the processes and requirements to ensure the efficient implementation of the Memorandum of Agreement (MOA).

f. DOE O 481.1C, *Work For Others (Non-Department of Energy Funded Work)*, dated 1-24-05, which establishes the policy, responsibilities, and procedures for authorizing and administering work for non- DOE entities by DOE/National Nuclear Security Administration (NNSA) and/or their respective contractor personnel or the use of DOE/NNSA facilities that is not directly funded by DOE appropriations.

g. DOE O 412.1A, *Work Authorization System*, dated 4-21-05, which provides the policy, responsibilities, and procedures for authorizing and administering DOE-funded work performed under DOE contracts.

h. DOE M 481.1-1A Chg 1, *Reimbursable Work for Non-Federal Sponsors Process Manual*, dated 9-28-01, provides detailed requirements to supplement DOE O 481.1C, *Work For Others (Non-Department of Energy Funded Work)*, dated 9-24-05, which establishes requirements for the performance of work for non- DOE/non- NNSA entities by DOE/NNSA/contractor personnel and/or the use of DOE/NNSA facilities that is not directly funded by DOE/NNSA appropriations.

i. DOE M 483.1-1, *DOE Cooperative Research and Development Agreements Manual*, dated 1-12-01, which provides detailed requirements to supplement DOE O 483.1, *DOE Cooperative Research and Development Agreements*, dated 1-12-01, which establishes requirements for the performance of technology transfer through the use of Cooperative Research and Development Agreements (CRADAs).

j. 10 CFR 600, *DOE Financial Assistance Rules*, which provides the policies and procedures for administration and management of all DOE financial assistance activities.

k. 10 CFR 602, *Epidemiology and Other Health Studies Financial Assistance*, which sets forth the policies and procedures applicable to the award and administration of financial assistance agreements and cooperative agreements for health-related research, education/training, conferences, communication, and related activities.

l. 10 CFR 605, *Office of Science Financial Assistance Program*, which provides policies and procedures for the administration and management of basic and applied research financial award agreements awarded by the Office of Science.

m. 10 CFR 745, *Protection of Human Subjects*, which sets out Federal requirements for DOE for the protection of human subjects involved in research activities.

n. 45 CFR 46, *Protection of Human Subjects*, Subparts B, C, and D, which sets out DOE-prescribed DHHS requirements for protected classes of human research subjects.

8. CONTACT. Questions regarding this Order should be addressed to the Program manager, DOE HSR Program, at the Office of Science, telephone 301-903-3213. Information about the DOE HSR protection program may be found at http://www.science.doe.gov/ober/humsubj/.

BY ORDER OF THE SECRETARY OF ENERGY:

CLAY SELL
Deputy Secretary

DEPARTMENTAL ELEMENTS TO WHICH DOE O 443.1A IS APPLICABLE

Office of the Secretary
Departmental Representative to the Defense Nuclear Facilities Safety Board
National Nuclear Security Administration
Office of the Chief Financial Officer
Office of the Chief Information Officer
Office of Civilian Radioactive Waste Management
Office of Congressional and Intergovernmental Affairs
Office of Economic Impact and Diversity
Office of Electricity Delivery and Energy Reliability
Office of Energy Efficiency and Renewable Energy
Office of Energy Information Administration
Office of Environment, Safety and Health
Office of Environmental Management
Office of Fossil Energy
Office of General Counsel
Office of Hearings and Appeals
Office of Human Capital Management
Office of Inspector General
Office of Intelligence and Counterintelligence
Office of Legacy Management
Office of Management
Office of Nuclear Energy, Science and Technology
Office of Policy and International Affairs
Office of Public Affairs
Office of Science
Office of Security and Safety Performance Assurance
Secretary of Energy Advisory Board
Bonneville Power Administration
Southeastern Power Administration
Southwestern Power Administration
Western Area Power Administration

CONTRACTOR REQUIREMENTS DOCUMENT
DOE O 443.1A, PROTECTION OF HUMAN SUBJECTS

Regardless of the performer of the work, the contractor is responsible for compliance with the requirements of this CRD. The contractor is responsible for flowing down the requirements of this CRD to subcontracts at any tier to the extent necessary to ensure the contractor's compliance with the requirements.

As directed by the contracting officer, the contractor must—

1. Ensure that the DOE HSR Program manager is notified of any new HSR project involving:

   a. an institution without an established Institutional Review Board (IRB);

   b. a foreign country;

   c. the potential for significant controversy (e.g., negative press or reaction from stakeholder or oversight groups);

   d. research subjects in a protected class;

   e. the generation or use of classified or sensitive unclassified information; or.

   f. current or former DOE employees or Contractor employees.

2. Ensure that research involving human subjects conducted at the contractor-operated institution, with the contractor's DOE-contract funding, or by contractor personnel is conducted in accordance with the applicable requirements of 10 CFR 745 and 45 CFR 46.

3. Ensure that contractor-issued solicitations or proposals for research, studies, tests, surveys, surveillance, or other data collection are reviewed to identify research involving human subjects.

4. Ensure that no research involving human subjects conducted at the contractor-operated institution, with the contractor's DOE-contract funding, or by contractor personnel is initiated without prior IRB approval under the terms of an approved assurance covering the research.

5. Maintain a current Federalwide Assurance (FWA) covering proposed and ongoing human subjects research (HSR).

6. Ensure that research is reviewed at intervals appropriate to the degree of risk, but not less than once per year, to assess the risk to test subjects and to assure the risk is reasonable in relation to anticipated benefits.

7. Periodically conduct self-assessments to ensure compliance with the HSR Program procedures and other requirements.

8. Prepare and submit an annual report for the DOE HSR Projects Database in accordance with directions and schedules provided by SC23.2 and the contracting officer.

9. Report the following to HSR Program manager (and any designated PSO, NNSA Administrators or HFO point of contact):

   a. any significant adverse events, unanticipated risks; and complaints about the research, with a description of any corrective actions taken and/or to be taken;

   b. any changes in the IRB membership;

   c. any suspension or termination of IRB approval of research;

   d. any significant non-compliance with HSR Program procedures or other requirements.

   NOTE: The adverse effects of any study are to be reported to the IRB for evaluation for further action with HSR Program manager, the PSO, the NNSA Administrators and the HFO, if necessary.)

10. Submit requests for waivers from these requirements in writing through the contracting officer to SC23.2, with appropriate justification.

11. Actively participate in HSR educational programs.